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Role of Irradiation in Management of Synovial Sarcoma: St. Jude Children's Research Hospital Experience

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The role of irradiation in the management of synovial sarcoma (SS) in pediatric patients is evaluated. The review covers all children seen at St. Jude Children's Research Hospital between May 1969 and December 1992 with the diagnosis of soft tissue sarcoma, of the 37 patients with the subtype SS, 16 received irradiation for the management of primary site disease. There were four IRS Group I, six Group II, four Group III, and two Group IV patients receiving irradiation. Tumor grade included seven Grade II and nine Grade III lesions. TMN staging identified eight T1 and eight T2 lesions. Follow-up has ranged from 14 to 117 months (med = 33 months). All IRS Group I patients had documented local control. Five of six IRS Group II and 4/4 Group III patients have had documented local control at last follow-up. IRS Group IV patients had either local control tumor stabilization (n = 1) or evidence of tumor regression (n = 1) at autopsy. Complications following irradiation include wound dehiscence (n = 1), surgery to revise a painful scar (n = 1) extremity length discrepancy (n = 2), and femoral head avascular necrosis (n = 1). At last follow-up, 10 of 14 patients receiving curative intent irradiation remain alive. This review indicates questionable benefit to the addition of irradiation for patients with adequate surgical resection and having "good" tumor characteristics (Grade I, II; IRS Group I, TMN T_{1A}, T_{1B}). For lesions that have had incomplete resection or partial response to chemotherapy, there is evidence that irradiation may provide durable local control. The role of irradiation in those patients with IRS Group IV disease is at present confined to palliative roles until the time when more effective chemotherapy will mandate the decision to treat primary disease for curative measures.

Key words: synovial sarcoma, irradiation, soft tissue sarcoma

INTRODUCTION

Synovial sarcoma (SS) is one of the most commonly diagnosed nonrhabdomyosarcoma soft tissue sarcomas (NRSTS) [1,2]. This tumor, which is characterized by the presence of epithelial-like spindle cells [3], is most frequently seen in tendon sheaths and joint capsules in adolescents and young adults [4]. Clinicopathological features, including a recent report on the influence of histological grade on survival, have been reported [5–7], yet there is little information on the role of irradiation in the treatment of SS [8–10]. We report a retrospective analysis of the role of irradiation in the initial treatment of newly diagnosed SS. Based on this experience, further recommendations concerning the role for irradiation will be made.

MATERIALS AND METHODS

Between May 1962 and December 1992, 40 patients with the diagnosis of SS were seen at St. Jude Children's Research Hospital (SJCRH). Three patients were seen as consultative cases without being treated and are excluded from this review. Sixteen of the remaining 37 received irradiation, 14 as part of initial management and two at the time of locally progressive disease. Ages at diagnosis ranged from 6½ to 22 years (median = 12½ years) (Table I). Primary disease sites included lower extremity (proximal n = 6, distal n = 4), upper extremity proximal (n = 2) or distal (n = 1), trunk (n = 2), and neck

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TABLE I. Patient and Irradiation Characteristics (n = 16)

Male: n = 8	
Female: n = 8	
Age at diagnosis: 6½–22 years (median = 12½ years)	
Radiation treatment	
External beam irradiation	n = 12
External beam irradiation + brachytherapy	n = 3
Brachytherapy alone	n = 1
Microscopic residual disease at irradiation	n = 11
Gross residual disease at irradiation	n = 5
Total dose 37.5–90 Gy (median 54 Gy)	

TABLE II Tumor Characteristics of Patients Receiving Irradiation

IRS group	Grades 1–2		Grade 3	
I	1		1	2
II	4	1		1
III		1		3
IV		1		1
	T_1	T_2	T_1	T_2

(n = 1). Follow-up has been maintained for all patients and has ranged from 14 to 117 months from the time of completion of irradiation (median = 33 months).

Pathological diagnosis was reviewed and confirmed in each case by the same individual (DP) using previously described criteria [11]. Seven tumors were classified as Grade II and 9 were Grade III according to the pediatric oncology group grading system [12]. Retrospective staging using the TMN and IRS staging systems was performed for all patients; eight of 19 T_1 and eight of 18 T_2 lesions received irradiation. Four of 22 IRS Group I, all IRS Groups II (n = 6) and III (n = 4), and two of five IRS Group IV patients received irradiation (Table II). Total doses ranged from 37.5 to 90 Gy (median = 54 Gy). Treatments were given once daily for 13 children (utilizing 160–180 cGy fraction) or twice daily using 110–120 cGy/fraction for two children. One patient received irradiation using only brachytherapy; three children received part (n = 3) of their irradiation utilizing brachytherapy techniques. Five patients had gross residual disease at the initiation of irradiation; 11 had microscopic residual disease. Statistical evaluation of various tumor characteristics (i.e., IRS Group, TMN Stage, and Grade) and treatment parameters were evaluated with the Kaplan Meier technique to determine impact, if any, on local control or survival.

RESULTS

Local Control

Local control within the irradiation volume has been maintained in 11 of 12 IRS Groups I–III patients who received irradiation as part of the initial planned management. Both patients who had evidence of locally recurrent disease following initial management with surgery alone (n = 1) or in conjunction with chemotherapy (n = 1) have been locally controlled at last follow-up. Time from completion of irradiation to last follow-up has ranged from 14 to 117 months (median = 33). Four of six patients with gross residual disease and all 11 receiving treatment for microscopic residual had local control. The two patients receiving irradiation for palliation (IRS Group IV) had evidence on autopsy of disease stabilization or disease reduction, which was also noted on physical exam and radiographic imaging prior to death.

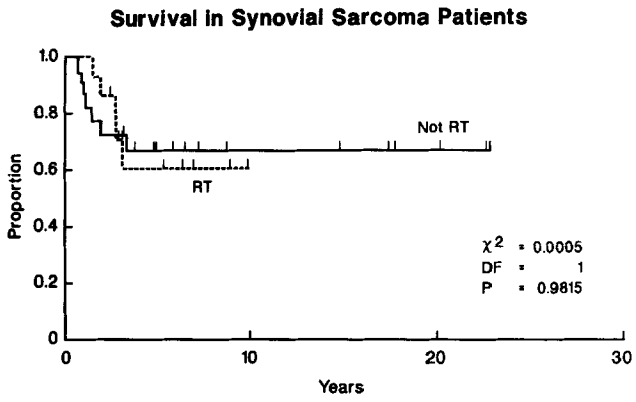

Fig. 1. Survival of irradiated vs. nonirradiated patients.

The sole local failure occurred in an IRS Group II patient with a distal extremity lesion (T_{2B}, Grade III). This patient, who refused chemotherapy, had gross total resection followed by interstitial brachytherapy to the tumor bed (22.5 Gy) and external beam irradiation, which delivered a total dose of 67.5 Gy. Eight months post-XRT, lung metastasis were found. Eighteen months post-XRT local recurrence was proven. This patient expired 27 months postirradiation.

Survival

Ten of 14 patients who received curative intent irradiation were alive at last follow-up. This includes 3 of 4 IRS Group I, 5 of 6 IRS Group II, and 2 of 4 IRS Group III patients. One of 11 with microscopic residual disease and 3 of 5 with gross residual disease at the initiation of irradiation have died. The four deaths were attributed to local and distant failure (n = 1) or distant failure (n = 3). Statistical evaluation did not demonstrate survival advantage for those receiving irradiation (P = .9) (Fig. 1).

Complications

All patients had evidence of acute epithelial reaction following completion of irradiation. There were no other reported acute or subacute reactions in any patient. Five patients developed significant late complications. One patient developed wound dehiscence 15 months after completion of irradiation following trauma to the site of

irradiation. This patient, who received interstitial irradiation alone to a total dose of 54 Gy delivered at 40 cGy/hr, has recovered full function following conservative management. One patient who required forequarter amputation for advanced local disease and subsequently received brachytherapy and external beam irradiation had revision of a painful scar 13 months postirradiation. Pathology documented no evidence of residual disease. One patient postirradiation developed an avascular necrosis of the left femoral head 57 months postirradiation, and two patients with lower extremity lesions had extremity length discrepancies noted >3 years after irradiation.

DISCUSSION

Treatment of pediatric NRSTS, which comprise 50% of all pediatric soft tissue sarcomas and 3% of all pediatric malignancies (11)m continues to undergo evaluation in an effort to better define prognostic factors and treatment modalities that may result in improved local control and survival [2,4,6,7]. Recent view regarding prognostic factors (i.e., tumor grade and size, biphasic versus monophasic, presence of metastatic disease at diagnosis) reported wide variations in subsequent local control, disease-free survival, and survival [5,10,12,14,15]. Because of these discrepancies, we decided to evaluate the role of irradiation in newly diagnosed SS based on the St. Jude Children's Research Hospital experience. Because few institutions treat significant numbers of NRSTS, much of the available information regarding treatment outcome on subtypes such as SS comes from multi-institutional trials.

Schmidt et al. [10] reported a series of 35 children from the Kiel Pediatric Tumor Registry diagnosed with SS. There were 21 biphasic and 14 monophasic lesions. The 7-year survival rate is reported at 63% for a selective subgroup of children treated with specific German pediatric soft tissue sarcoma protocols (CWS 81/86 trials). However, there was no information indicating whether the use of irradiation or the disease status at the initiation of irradiation (gross vs. microscopic) had any influence on development of local control and eventual survival.

The issue of disease status at the initiation of irradiation was addressed by Carson et al. [8] in a report of 36 patients from the Princess Margaret Hospital. In this series, 16 patients were treated with primary irradiation as part of the initial management of their newly diagnosed SS. Eleven of 16 of these patients had long-term local control following the use of irradiation and surgery. However, 7 of 7 with microscopic residual disease had long-term local control compared with 4 of 9 patients who received biopsy only or incomplete surgical resection resulting in gross residual disease the time of irradiation initiation. Dose of irradiation for those patients who obtained local control ranged between 24 and 120 Gy. This is similar to the present series where 11 of 12 patients receiving irradiation for primary treatment have maintained continuous local disease-free control.

Based on the view of these limited series, it would appear that irradiation may play a role in the treatment of patents with newly diagnosed SS, especially for those children with minimal residual primary disease following surgery. Our series raises questions as to the benefit of irradiation for those patients who have had complete surgical resection (Grade I, II; IRS Group I; TMN T_{1A}, T_{1B}). However, for lesions that have had incomplete resection or biopsy only or have had only partial response to chemotherapy, evidence would appear to support use of irradiation in an attempt to improve local control rates. We currently utilize hyperfractionated external beam irradiation for those children with bulky residual disease using 110–120 cGy/fraction given b.i.d. separated by 6 hours. We currently use total doses of between 50–66 Gy for these lesions. When possible, brachytherpy is used as initial therapy to surgical sites harboring microscopic residual disease. We deliver 20–25 Gy to a 1 cm margin delivering 40 cGy/hr. This is then supplemented by conventional once-daily irradiation of 180 cGy/fraction. We routinely use 3–5 cm margins around the original tumor volume to define the radiation portal. The role of irradiation in those patients with IRS Group IV disease is at the present time confined to palliative roles until the time when more effective chemotherapy will mandate the decision to treat primary disease for curative measures.

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